REMARKS

THE CLAIM AMENDMENT

Claims 1 and 32 have been amended to more fully define the invention. Claim 12 has been amended to remove the term "comprising." Claims 1, 32, and 35 include amendments to change the claim term "prevents" to the claim term "disrupts." Support for the recitation that the blocking sequence "disrupts" secondary structure formation is found throughout the specification, for example, in the title and paragraphs 0008, 0053, 0054, 0063, 0069, Example 1 (paras. 0102 and 0103), and Example 2 (para. 0104). No new matter has been added to the application with the claim amendments made herein.

RESPONSE TO THE EXAMINER'S RESPONSE TO APPLICANTS' ARGUMENTS

The discussions below set forth applicants position on the Examiner's misinterpretation of the blocking sequence as non-structural and therefore, applicants will not repeat their position here; however, applicants are taking this opportunity to address two other statements that the Examiner makes in her response to applicants' arguments that are not proper.

At the top of page 15 of the Office Action, the Examiner asserts that applicants do not define the term "substantially." This statement is not accurate. The term "substantially" is used in clause (b) of claims 1 and 32 to modify the word "complementary" to form the claim term "substantially complementary." The claim term "substantially complementary" is expressly defined at paragraph 0042 of the specification (page 11) to mean at least about 80% complementarity between the nucleotides of the two strands in question.

Also at the top of page 15 of the Office Action, the Examiner asserts that there is no requirement in the claims that the target nucleic acid have secondary structure. This statement is also not accurate. It is a well-known claim construction principle that claims can positively recite claim limitations or they can inferentially recite claim limitations. In either case, it is axiomatic that every recited claim limitation ***must*** be considered as part of the claim since it is the claim limitations that define the invention. *See, e.g., General Foods Corp. v. Studiengesellschaft Köhle mbH*, 972 F.2d 1272 (Fed. Cir. 1992) ("..patent claims must be read *as a whole*…" (emphasis added by the Court)). In pre-amendment claims 1 and 32, the secondary structure was recited as an inferential claim limitation of the target molecular and thus, the secondary structures was a claim limitation that was a necessary and integral part of the claim.

With this paper, claims 1 and 32 have been amended to positively recite that the target molecule comprises a secondary structure forming region. Applicants submit that the amendment to the claims does not change the scope of the claims and is made solely to clarify the scope of the claims and further

define the claim limitations in order to facilitate the Examiner's further consideration of the claimed invention.

CLAIM REJECTION UNDER 35 U.S.C. § 102(b) BY WILTON ET AL.

Claims 1-5, 9, 12-14, and 26 stand rejected under 35 U.S.C. § 102(b) as anticipated by Wilton et al. This rejection is respectfully traversed.

The *prima facie* case is a procedural tool which, as used in patent examination, means not only that the evidence of the prior art would reasonably allow the conclusion the Examiner seeks, but also that the prior art compels such a conclusion if the applicant produces no evidence or argument to rebut it. *In re Spada,* 911 F.2d 705 (Fed. Cir. 1990). If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more, the applicant is entitled to a grant of the patent. *In re Oetiker,* 977 F.2d 1443 (Fed. Cir. 1992).

Where the Examiner's *prima facie* case is premised on anticipation rejections, the Examiner must show that ***each and every element*** of the claimed invention is found, either expressly or inherently, in a single prior art reference. *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565, 24 USPQ2d 1321, 1326 (Fed. Cir. 1992) (emphasis added here).

In the Office Action under reply, the Examiner maintains that clause (b) of claim 1 is "functional language that imparts no structural limitations to the nucleic acid." Applicants respectfully disagree for the reasons set forth in the prior responses and herein.

As recited in claim 1, the claimed invention is a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region. The primer of claim 1 is positively recited as comprising two elements: (a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region; and (b) a blocking sequence substantially complementary to a segment of the secondary structure forming region.

As noted above, the Examiner states that clause (b) of claim 1 imparts no structural limitations to the nucleic acid. On this matter, applicants submit that the language of clause (b) is not intended to be a limitation of the target nucleotide sequence of the target molecule; rather, clause (b) represents a limitation of the claimed dual-purpose primer. Because the recitation of the blocking sequence (as well as the primer sequence) follows the phrase "the primer comprises," it follows that the primer sequence and the blocking sequence are what comprise the dual-purpose primer. In view of the foregoing, it is

unarguable that the language of clause (b) is a limitation of the claimed dual-purpose primer and *not* the target nucleotide sequence of the target molecule.

Notwithstanding the foregoing, in each of the Office Actions, the Examiner has held the position that the blocking sequence is a functional feature that is not given any patentable weight. The Examiner, however, has never provided applicants with a reason for the Examiner's refusal to acknowledge the blocking sequence as a structural limitation; in each of the prior responses, the Examiner merely states that the blocking sequence is functional language. As previously discussed, the Examiner's failure to give weight to the blocking sequence is improper and should not be maintained for at least the following reasons.

As noted above, claim 1 has been amended to more clearly define the structural feature of the blocking sequence. Directing the Examiner's attention to Figure 5, which is a schematic representation of the dual-purpose primer of the present invention, the blocker region of the primer B is clearly shown as a part of the SNPdragon primer. As is shown therein, the blocker region B is designed to bind to the region on the target nucleotide B′ that needs to be blocked in order to allow the SNP site X to be detected through the primer region P (*see also*, paragraphs 0019 and 0057). Figure 10 shows an additional schematic representation of the dual-purpose primers of the present invention. In Figure 10, the SNP site is within a secondary structure forming region and thus, is not available for detection and amplification. By hybridizing to a segment within the secondary structure forming region, the blocking sequence of the dual-purpose primer of the present invention is able to disrupt the secondary structure forming region thus allowing the ligation portion of the dual-purpose primer to hybridize to the SNP thereby making the amplification of the SNP site possible.

As shown in both Figures 5 and 10, the blocking sequence is a separate portion of the dual purpose primer of the present invention, which may be adjacent to the priming sequence or separated from the priming sequence by a spacer. Without the blocking sequence, the primer of the present invention would not be able to carry out its dual purpose, specifically, to block formation of secondary structure and to prime the SNP of interest.

Figures 4, 6, and 8 show the surprising and unexpected results that the dual-purpose primers of the present invention have on the detection of the SNP in exon 1 of the cytochrome P450 CYP2D6 gene. In Figure 4, detection of exon 1 is measured at less than 10.0 with the conventional primer and in excess of 120.0 with the dual-purpose primer of the present invention (*see also*, paragraph 0018). In Figure 6, a 250 bp band for exon 1 is detected using the dual-purpose primer of the present invention with blocking sequences of 8, 10, and 12 nucleotides, but the band is barely detectable when the blocking sequence is not included in the primer (*see also*, paragraphs 0020, 0057, and 0095). In Figure 8, exon 1 is assayed for

detection with the following three primers: (i) the dual-purpose primers of the present invention having blocking sequence of 8, 10, and 12 nucleotides; (ii) convention primers; and (iii) convention primers having an external blocker of 25 nucleotides (*see*, paragraph 0096). As shown therein, the conventional primers do not show any appreciable detection of exon 1. While the conventional primers with the external blocker do show detection, the dual-purpose primers with the 10 and most notably with the 12 nucleotide blocking sequences show enhanced detection over the conventional primers with the 25 nucleotide external blocker.

The foregoing discussion of the present invention clearly shows that the blocking sequence is an integral structural feature of the claimed dual-purpose primers. The Examiner's failure to appreciate the blocking sequence as a structural feature of the claimed dual-purposes primers is difficult for applicants to grasp as the specification clearly provides detailed disclosure, figures, and examples showing the surprising and unexpected effects that the blocking sequence has on the identification of SNPs that are proximal to or contained within secondary structure forming regions. In this respect, applicants respectfully request the Examiner's reconsideration of the claims with the blocking sequence as a structural part of the claimed dual-purpose primers. Should the Examiner choose to maintain that the blocking sequence does not exist as a structural feature of the claimed dual-purpose primers, applicants respectfully request that the Examiner provide applicants with the Examiner's rationale for so holding.

Turning back to the claims under rejection, as set forth in claim 1, the claimed invention requires that the target nucleotide sequence (such as for example an SNP) is proximal to or contained within a secondary structure forming region of the target molecule. When the target molecule has such a configuration, the dual purpose primers are able to disrupt the secondary structure forming region of the target molecule so that the primer can detect and amplify the target nucleotide sequence.

Turning to the cited reference, as explained in the prior responses, Wilton et al. expressly teach primers that are designed to form secondary structures in order to facilitate detection of the genes in question. The primers of Wilton et al. are shown in Figure 1. As stated in the Figure 1 legend, the snapback primers (Primer SB B(r) and Primer SB D(r)) are distinguished from the conventional primers by the additional 11 bases complementary to the sequence around the mdx mutation.

Because the Examiner is failing to give patentable weight to the blocking sequence of clause (b) of claim 1, the Examiner's analysis stops at the disclosure of the Wilton et al. snapback primers shown in Figure 1 on the mistaken assumption that the 11 bases complementary to the segment of the target nucleotide of interest arguably satisfies the limitations of clause (a) of claim 1. Proper consideration of the blocking sequence of clause (b) will show the impropriety of the Examiner's position.

As discussed in Wilton et al. at page 254, col. 2 (first full paragraph), PCR *products* generated from a forward primer and either of the snapback primers have terminal sequences that when in single-stranded form reanneal or snapback to the area under investigation; in other words, the 3′ terminus of the forward strand or the 5′ terminus of the reverse strand have the potential to reanneal to the region of the mdx mutation, thus forming a secondary structure (*see*, page 256, col.2).

As claimed and as explained above, the claimed invention requires that the target nucleotide sequence is proximal to or contained within a secondary structure forming region. When the target molecule has such a configuration, the blocking sequence is capable of disrupting the secondary structure forming region so that the primer may detect and amplify the target nucleic acid; thus, unlike Wilton et al. where the reannealing of the oligonucleotide to form the secondary structure formation occurs *after* a priming cycle is complete, with the claimed invention, priming of the target nucleotide segment cannot *begin* until the secondary structure formation is disrupted.

With respect to the Examiner's comments regarding the dependent claims, applicants have the following comments. The Examiner's analysis for claim 5 appears to equate the 11 bases of the Wilton et al. primer to the non-hybridizing spacer of the present invention. Applicants submit that the non-hybridizing spacer of the present invention is not comparable to the 11 bases of the Wilton et al. primer. As is shown in Figure 3 of Wilton et al., the 11 bases are bases complementary to the sequence around the mdx mutation that are intended to reanneal to the dystrophin sequence. By contrast, as shown in Figures 5 and 10 of the instant application, the spacer sequence does not reanneal to the primer, rather, its function is strictly to separate the primer sequence from the blocking sequence.

Regarding the Examiner's analysis of claim 12, the Examiner asserts that the spacer of Wilton et al. is comprised of the single recurring nucleotide A and references SB-B(r) and SB-D(r) of Table 1. Applicants do not follow the Examiner's analysis of this claim. In the analysis of claim 5, the Examiner asserts that the 11 base pair sequence in the non-hybridizing sequence; the 11 base pair sequence is set forth in Figure 1, Table 1, and Figure 3 as GCAACAAAATG. That the 11 base pair sequence includes a recurring nucleotide is not a disclosure that is comparable to the single nucleotide space of the claimed invention. As stated above, Wilton et al. expressly teaches the 11 base pair segment as being comparable to the sequence around the mdx mutation that can anneal back to the normal dystrophin sequence. Within this context, logically, a spacer sequence would have to be a sequence that would separate the two sequences that anneal to each other. On this matter, Wilton et al. do *not* teach or suggest a spacer that is a recurring single nucleotide.

Regarding the Examiner's analysis of claims 13 and 14, the Examiner asserts that the means for language in claim 13 and the arresting linker of claim 14 are functional language. Applicants disagree. It

is well-established law the means for claims are interpreted to include the structures disclosed in the specification. *See, e.g., Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558 (Fed. Cir. 2000) (en banc) ("A claim element recited in means-plus-function language literally encompasses the corresponding structure and its equivalents…In contrast, a claim element that recites the corresponding structure does not literally encompass equivalents of that structure."). In this respect, applicants direct the Examiner's attention to paragraph 0059 of the specification (page 15) where the means for halting transcription is defined generally as "a linker joining the two primer segments that prevents the polymerase used from continuing replication across the probe sequences – nucleotide spacer junction." The paragraph explains that the means for halting transcription includes arresting linkers and the remainder of paragraph 0059 provides examples of arresting linkers. Further, the term "arresting linker" is expressly defined at paragraph 0043 (page 11) as "a nucleotidic or non-nucleotidic linker, in a probe or primer, which is not amplified by the amplification enzyme." In view of the foregoing, applicants submit that claims 13 and 14 do not recite functional language, but in fact recite structural limitations that must be considered by the Examiner.

Because Wilton et al. do not teach or suggest that the primers disclosed therein include a blocking sequence that is substantially complementary to segment of a secondary structure forming region, it follows that Wilton et al. do not anticipate the claimed invention. Because Wilton et al. do not anticipate the claimed invention, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 102(b) BY BANNWARTH ET AL.

Claims 1, 2, and 4-7 stand rejected under 35 U.S.C. § 102(b) as anticipated by Bannwarth et al. This rejection is respectfully traversed for the same reasons set forth above in the discussion of Wilton et al. and for the additional reasons set forth below.

As explained in the responses filed on November 8, 2006, and July 27, 2007, Bannwarth et al. teach a self-complementary oligonucleotide that backfolds upon itself in order to form a double-stranded section; the oligonucleotide formed in Bannwarth et al. is similar to the PCR product produced in Wilton et al. At col. 2, ll. 17-34, of Bannwarth et al., the structure of the oligonucleotide is described; specifically, the oligonucleotide consists of a sequence substantially complementary to a segment of a target nucleic acid (Pp); a non-nucleotidic linking sequence (L), which serves to facilitate the backfolding; a sequence substantially complementary to Pp (Pc); and an energy source (X), which is used for detecting the oligonucleotide via energy transfer when the oligonucleotide is put in contact with a detection oligonucleotide. Figure 1 of Bannwarth et al. shows the configuration of the oligonucleotide

when the Pp and Pc complementary strands anneal to form the double-stranded self-complementary oligonucleotide disclosed therein.

As in the Wilton et al. rejection, the Examiner is taking the position that the language of clause (b) of claim 1 is functional language that has no patentable weight. By failing to give any patentable weight to the blocking sequence of clause (b), the Examiner is able to take the position that Bannwarth et al. anticipates the claims because it discloses an oligonucleotide with a sequence substantially complementary to a segment of a target nucleic acid (Pp). Proper consideration of the blocking sequence of clause (b) will show the impropriety of the Examiner's position.

As set forth above, the claimed invention requires that the target nucleotide sequence in question is proximal to or contained within a secondary structure forming region of the target molecule. When the target molecule has such a configuration, the blocking sequence of the dual purpose primer of the claimed invention is able to disrupt the secondary structure forming region of the target molecule so that the primer sequence can detect and amplify the target nucleotide sequence.

As discussed above, all that Bannwarth et al. teach is an oligonucleotide that has a sequence that is complementary to a segment of a target nucleic acid Pp and a sequence Pc that is complementary to the sequence Pp, wherein the oligonucleotide backfolds upon itself via a non-nucleotidic linker L when Pp and Pc hybridize. Bannwarth et al. do not teach or suggest that the segment of the target nucleic acid is proximal to or contained within a secondary structure forming region of the target molecule or that the oligonucleotide disclosed therein has a blocking sequence substantially complementary to a segment of a secondary structure forming region of the target nucleic acid. Without such a teaching or suggestion, it follows that Bannwarth et al. cannot anticipate the claimed invention.

Because Bannwarth et al. do not anticipate the claimed invention for the reasons set forth above, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 102(b) BY LAIBINIS ET AL.

Claims 1 and 5-8 stand rejected as anticipated under 35 U.S.C. § 102(b) by Laibinis et al. This rejection is respectfully traversed for the same reasons set forth above in the discussion of Wilton et al. and for the additional reasons set forth below.

As explained in the response filed on November 8, 2006, and July 27, 2007, Laibinis et al. teach a method for covalently linking a nucleic acid molecule having a target moiety to a support-bound oligonucleotide (i.e., a capture probe). The nucleic acid molecule is hybridized to the capture probe via a complementary sequence, i.e., a pairing sequence on the nucleic acid molecule, which is covalently bound to a complementary sequence on the capture probe (para. 0010). The only mention in Laibinis et al. with

respect to secondary or tertiary structure is at paragraph 0032 where it is stated that the target moiety may include secondary or tertiary structure. Laibinis et al.; however, does *not* suggest that the structures may be problematic and does *not* contemplate any reason or way to disrupt the secondary structure.

With this rejection, the Examiner asserts that the claim term "primer" in clause (a) of claim 1, in addition to all of clause (b) of claim 1, are functional recitations that are given no patentable weight (Office Action, page 6, item 6, 3rd and 4th paragraphs). The Examiner provides no reason for asserting the claim term "primer" as functional language in this rejection, but not in the other rejections. Without a reason for asserting that the claim term "primer" is functional language, applicants are unable to respond to the Examiner's statement. Notwithstanding the foregoing, as the claim is directed to a primer, specifically a dual-purpose primer, and it positively recites two claim limitations that give structure to the primer, it would appear that the ordinary artisan would readily interpret the dual-purpose primer of the claimed invention to be a composition with a defined structure. Should the Examiner maintain that the claim term "primer" is functional language, applicants respectfully request that the Examiner provide applicants with the Examiner's rationale for so holding.

Turning to the substance of the Examiner's rejection, by failing to give any patentable weight to the claim term "primer" and to the language of clause (b), the Examiner is able to take the position that Laibinis et al. anticipates the claims because it discloses the hybridization of a target sequence to a complementary sequence on a capture probe. Proper consideration of the primer of clause (a) and the blocking sequence of clause (b) will show the impropriety of the Examiner's position.

As set forth above, the claimed invention requires that the target nucleotide sequence in question is proximal to or contained within a secondary structure forming region of the target molecule. When the target molecule has such a configuration, the dual purpose primers are able to disrupt the secondary structure forming region of the target molecule so that the primer can detect and amplify the target nucleotide sequence.

As discussed above, all that Laibinis et al. teach is the covalent bonding of a capture probe to a nucleic acid probe via complementary sequences. Laibinis et al. do not teach or suggest that a segment of the target nucleic acid is proximal to or contained within a secondary structure forming region of the target molecule or that the oligonucleotide disclosed therein has a blocking sequence substantially complementary to a segment of a secondary structure forming region of the target nucleic acid. Without such a teaching or suggestion, it follows that Laibinis et al. cannot anticipate the claimed invention.

Because Laibinis et al. do not anticipate the claimed invention for the reasons set forth above, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 102(b) BY BEATTIE ET AL.

Claims 1, 17, and 18 stand rejected as anticipated under 35 U.S.C. § 102(b) by Laibinis et al. respectfully traversed for the same reasons set forth above in the discussion of Wilton et al. and for the additional reasons set forth below.

As explained in the response filed on November 8, 2006 (applicants inadvertently omitted their arguments in traverse of the anticipation of Beattie et al. in the response filed on July 27, 2007), Beattie et al. teach tandem hybridization techniques to address various problems associated with nucleic acid hybridizations including the spontaneous formation of secondary structures in the single-stranded target nucleic acid. The difference between the dual-purpose primers of the present invention and the tandem hybridization technique described in Beattie et al. are most evident when Figures 5 and 10 of the instant application are compared against Figures 13A, 13B, 14A, 14B, 15A, and 15B of Beattie et al. Figures 5 and 10 of the instant application are explained above under the discussion of Wilton et al. By contrast, as shown in Figures 13A and 13B of Beattie et al., the hybridization technique of Beattie et al. includes hybridization of a molar excess of labeled oligonucleotides in tandem to a heat-denatured target strand of a double-stranded target DNA (*see also*, col. 7, l.66, to col. 8, l.8). As is shown in Figures 14A and 14B, the probes of Beattie et al. do ***not*** have blocking sequences. Further, as is clear from Figures 13 to 15, as well as the text of Beattie et al., the Beattie et al. probes are intended only to identify the sequence of a target analyte and not to amplify the target strand.

With this rejection, the Examiner again asserts that the claim term "primer" in clause (a) of claim 1, in addition to all of clause (b) of claim 1, are functional recitations that are given no patentable weight (Office Action, page 6, item 67, 3rd and 4th paragraphs). By failing to give any patentable weight to the claim term "primer" and to the language of clause (b), the Examiner is able to take the position that Beattie et al. anticipates the claims because it discloses the hybridization of oligonucleotides to a target strand of DNA. Proper consideration of the primer of clause (a) and the blocking sequence of clause (b) will show the impropriety of the Examiner's position.

As set forth above, the claimed invention requires that the target nucleotide sequence in question is proximal to or contained within a secondary structure forming region of the target molecule. When the target molecule has such a configuration, the dual purpose primers are able to disrupt the secondary structure forming region of the target molecule so that the primer can detect and amplify the target nucleotide sequence.

As discussed above, Beattie et al. teach the tandem hybridization of labeled oligonucleotides to a heat-denatured strand of double-stranded DNA in order to avoid the spontaneous formation of secondary structures in the single-stranded target nucleotide. Beattie et al. do not teach or suggest that a segment of

the target DNA is proximal to or contained within a secondary structure forming region of the target molecule or that the oligonucleotides disclosed therein have a blocking sequence substantially complementary to a segment of a secondary structure forming region of the target nucleic acid. Without such a teaching or suggestion, it follows that Beattie et al. cannot anticipate the claimed invention.

Because Beattie et al. do not anticipate the claimed invention for the reasons set forth above, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 103(a) OVER WILTON ET AL. IN VIEW OF STRATAGENE

Claims 27-30 stand rejected under 35 U.S.C. § 103(a) as obvious over Wilton et al. in view of the Stratagene Catalog. This rejection is respectfully traversed.

Claims 27-30 are kit claims that depend from claim 1. The primary reference, Wilton et al., is discussed above. The Examiner cites the Stratagene Catalog for the motivation to combine the reagents of claim 1 into a kit. Because the teachings of the Wilton et al. reference do not lead the ordinary artisan to the claimed invention, the teachings of a kit from the Stratagene Catalog will not serve to render obvious the invention as recited in claims 27-30.

Because the Examiner's hypothetical combination of Wilton et al. in view of the Stratagene Catalog does not render the claimed invention obvious, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 103(a) OVER BANNWARTH ET AL. IN VIEW OF STRATAGENE

Claim 28 stands rejected under 35 U.S.C. § 103(a) as obvious over Bannwarth et al. in view of the Stratagene Catalog. This rejection is respectfully traversed.

Claim 28 is a kit claim that ultimately depends from claim 1. The primary reference, Bannwarth et al., is discussed above. The Examiner cites the Stratagene Catalog for the motivation to combine the reagents of claim 1 into a kit. Because the teachings of the Bannwarth et al. reference do not lead the ordinary artisan to the claimed invention, the teachings of a kit from the Stratagene Catalog will not serve to render obvious the invention as recited in claim 28.

Because the Examiner's hypothetical combination of Bannwarth et al. in view of the Stratagene Catalog does not render the claimed invention obvious, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 103(a) OVER BEATTIE ET AL. IN VIEW OF STRATAGENE

Claims 28-34 stands rejected under 35 U.S.C. § 103(a) as obvious over Beattie et al. in view of the Stratagene Catalog. This rejection is respectfully traversed.

Claims 28 to 31 are kit claims that depend from claim 1. The primary reference, Beattie et al., is discussed above. The Examiner cites the Stratagene Catalog for the motivation to combine the reagents of claim 1 into a kit. Because the teachings of the Beattie et al. reference do not lead the ordinary artisan to the claimed invention, the teachings of a kit from the Stratagene Catalog will not serve to render obvious the invention as recited in claims 28-31.

Claims 32-34 are directed to a hybridization probe that has the same elements as claim 1; accordingly the discussion of Beattie et al. set forth for claim 1 applies with equal force to claims 32-34.

Because the Examiner's hypothetical combination of Beattie et al. in view of the Stratagene Catalog does not render the claimed invention obvious, applicants respectfully request withdrawal of this rejection.

CLAIM REJECTION - 35 U.S.C. § 103(a) OVER WILTON ET AL. IN VIEW OF FISHER

Claims 10, 11, 15, and 16 stand rejected under 35 U.S.C. § 103(a) as obvious over Wilton et al. in view of Fisher. This rejection is respectfully traversed.

Claims 10, 11, 15, and 15 depend from claim 1. The primary reference, Wilton et al., is discussed above. The Examiner cites Fisher for the teachings of the non-natural bases iso-cytosine and iso-guanine. Because Wilton et al. do not teach or suggest the invention as recited in claim 1, the additional teaching of Fisher will not serve to render obvious the invention as recited in dependent claims 10, 11, 15 and 16.

Because the Examiner's hypothetical combination of Wilton et al. in view of Fisher does not render the claimed invention obvious, applicants respectfully request withdrawal of this rejection.

CONCLUSION

With this paper, each of the Examiner's rejections have been fully addressed and overcome. Because there will be no outstanding issues for this matter upon entry of this paper, applicants respectfully request withdrawal of all claim rejections and passage of this application to issue. If the Examiner chooses to maintain the rejections, applicants request entry of the amendments set forth in this paper for purposes of placing the claims in better form for consideration on appeal pursuant to the provisions of 37 C.F.R. § 1.116(a)(2).

Any questions regarding this paper or the application in general may be addressed to the undersigned attorney at 650-320-7662 or karen@canaanlaw.com.

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